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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
EPPS FORD, JANET L	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 04/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/713,017	CHOULIKA ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford, Ph.D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,25,28 and 30-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.

4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5)☐ Notice of Informal Patent Application (PTO-152)

6)☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicant's amendment to claim 30 does not comply with 37 CFR 1.121(c), in particular in claim 30, line 1, Applicants inserted the term "28" after the term "claim," however there are no markings to indicated that the term "29" was deleted immediately after the term "claim" in line 1.

Response to Arguments

2. Applicant's arguments, see response, filed 7-06-04, with respect to the rejection(s)of claim(s) 1, 25, 28-38, and 40-45 under 35 USC 112, 1st paragraph or 35 USC 102(b) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made under 35 USC 103(a) over Gilboa et al. in view of Enquist et al.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claim 40 recites the limitation "29" in line 1. There is insufficient antecedent basis for this limitation in the claim since claim 29 was cancelled by Applicants in the response filed 7-06-04.

6. Claims 28 and 43 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 28 and 43 recite wherein the retroelements comprise a U3 region of a 3'LTR, a U5 region of a 5' LTR and further comprising an R region. However, neither claim 1 nor claim 25 provides sufficient antecedent basis for the limitation in claims 28 or 43 wherein the nucleotide sequence sequence of retroelements further comprise an R region. It is noted that this rejection was previously set forth in the Office Action mailed 7/25/03, however it was not addressed in the subsequent Office Action mailed 4/06/2004. **In the response filed 9/20/03, Applicants argued that by amending claims 28 and 43 to refer to the antecedent 3' LTR and 5' LTR in claims 25 and 1, they have over come this rejection. However, the amendment to the claims filed 9/20/03, did not overcome this rejection because it remains that independent claims 1 and 25 do not further comprise an R region beyond the 3' and/or 5' LTR sequence of retroelements, such the sequence of interest and the recombinase recognition sequence are incorporated into said R region. Moreover, it is unclear if the "R region," is a part of the 5' or 3' LTR recited in claims 1 and 25, or if the R region represents a region beyond the retroelements set forth in claims 1 and 25. Furthermore, claims 1 and 25 clearly state that the insertion sequence is located in the 3' and/or 5' LTR region.**

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1, 25, 28, 30-38, and 40-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gilboa et al. (WO 89/11539 A1) in view of Enquist et al. (EP300422A2), Anderson (US Patent No. 5,629,159) and Robertson et al. (US 5,225,337).

Claim 1 is drawn to a sequence of synthetic or natural retroelements, which comprises an insertion sequence incorporated in a region that can be transferred into a target cell and integrated into a recombinant provirus when said target cell is infected by a retrovirus comprising said sequence of retroelements; said insertion sequence comprises a nucleotide sequence of interest which can be integrated into the genome of the target cell, and a recombinase recognition sequence; said retroelements comprise a 3' and/or 5' LTR region and said insertion sequence is incorporated into said 3' LTR or 5' LTR.

Gilboa et al. describe the double copy retroviral vector, which comprises an insertion of the ADA gene sequence into the U3 region of a 3' LTR, see for example Figure 4, and page 13, lines 12-29. Additionally, Gilboa et al. generically describes: a retroviral vector for introducing into a eukaryotic cell DNA encoding a transcription unit which comprises a first DNA sequence which is the reverse transcript of at least a portion of a retrovirus, said portion including both the 5' LTR sequence and the 3' LTR sequence of the retrovirus, and a second DNA sequence encoding the transcription unit which is inserted into the U3 region of the 3' LTR sequence.

Gilboa et al. further teach that the second DNA sequence of the retroviral vector encoding encodes an RNA molecule, wherein the RNA encodes a recognition sequence for a DNA or RNA binding protein (see pages 46-47, claims 1, 10 and 12 of the Gilboa et al. WIPO document). Gilboa et al. does not teach wherein the recognition sequence is a recombinase recognition sequence, wherein the retroviral vector encodes a recombinase protein, or wherein the nucleotide sequence of interest is an antisense RNA or a ribozyme sequence.

Enquist discloses the desirability of using recombination as a means of modifying retroviral vectors (page 5, lines 43-57 and page 7, lines 26-39). A viral vector is modified by the insertion of loxP elements (page 5, lines 1-26) and the loxP element so included is a recognition sequence for the bacteriophage P1 Cre recombinase, which is disclosed as either inserting sequences into the viral vector, and/or removing sequences from the vector (page 9, lines 1-5). The sequence of interest may encode a polypeptide. Enquist et al. does not disclose such a viral vector wherein the Cre recombinase is encoded within the vector itself.

Anderson discloses retroviral vector constructions (see figures 1a-1d and 2a-b) which contain LTR elements that express sequences of interest that are integrated into a cis-acting region of the virus, encodes selectable markers, and which has promoters and other control elements. Such vectors were modified to contain loxP elements (fig. 2a-2b) for the removal of an intervening nucleotide sequence. The use of the Cre/loxP and FLP/FRT recombinase systems is disclosed (col. 7, lines 20-28) and the gene encoding the recombinase (either Cre or FLP) is part of the retroviral construct (col. 8, lines 38-56). The desirability of removing or eliminating the recombinase by the recombination event, along with a sequence of interest, is further

disclosed at col. 8, lines 47-52. At column 11, lines 41-67, the use of replication defective retroviral vectors is described in detail, along with methods of using the vectors.

Robertson et al. teach the design of a modified retroviral vector designed to encode a ribozyme sequence. In particular Robertson et al. teach that specific delivery of ribozymes into cells should be possible to achieve using retroviral technology. According to Robertson et al. defective retroviral vectors, which incorporate their own RNA sequence in the form of DNA into the host chromosome, will be engineered to incorporate modified ribozymes sequence into the host, where copies will be made and released into the cytoplasm to interact with the target nucleotide sequences.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of Gilboa et al. in view of Enquist et al., Anderson, and Robertson et al. to make the instant invention. In seeking alternative means to express a protein using retroviral vectors, one of skill in the art would have combined the teachings of Guild with regards to replication deficient retroviral vectors with the teachings of Enquist et al. with regard to the utility of recombination as a means of preparing and modifying vectors of all types, including retroviral vectors, for the known and expected property of effective insertion or removal of a sequence of interest into or from the vector. Additionally, one of ordinary skill in the art at the time of the instant invention would have been motivated to introduce recombinase recognition sites into the LTR regions of the vectors of Gilboa et al. since Gilboa et al. expressly contemplates the introduction of recognition sites for DNA or RNA binding proteins, and Enquist et al. describe the introduction of the 34 base pair recognition site (lox site) for the DNA binding protein, Cre recombinase. Furthermore, one of ordinary skill in the art at the time of the

instant invention would have been motivated to further combine the teachings of Anderson with regard to encoding the recombinase directly on the retroviral vector, for the known and expected property disclosed by Anderson, namely for the simultaneous removal of the recombinase enzyme along with the sequence of interest. In so doing, one of skill in the art would have prepared a recombinant vector that would integrate into the genome, wherein one could then inducibly (column 8, lines 38/55) remove sequences integrated into the genome by the retroviral vector, along with the recombinase. Finally, one of ordinary skill in the art at the time of the instant invention would have been motivated to modify the retroviral vectors of Gilboa et al. to comprise wherein the nucleotide sequence of interest encodes a ribozyme sequence because Robertson et al. teaches the desirability of utilizing retroviral vectors for specific delivery of ribozymes into cells. Given the teachings of the prior art and the knowledge of one of ordinary skill in the art, it must be considered that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention. Thus, the invention as a whole would have been *prima facie* obvious at the time the instant invention was made.

Allowable Subject Matter

9. Claim 39 is allowable over the prior art of searched.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford, Ph.D. whose telephone number is 571-272-0757. The examiner can normally be reached on Monday-Saturday, Flex Schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Janet L. Epps-Ford, Ph.D.
Patent Examiner
Art Unit 1635

JLE